REMARKS

Claims 87-100 are pending in the above-identified application, of which claims 97-100 are presently withdrawn from consideration. Support for the amendment reciting the cysteine backbone is found, e.g., at page 21, line 7, at page 26, line 29-page 27, line 1, and in Figure 1. Support for the amendment reciting altering bone density is found throughout the specification in numerous statements that inhibitors of this protein increase bone density, e.g. at pages 40-41, and page 48, lines 13-20.

A. The rejection under 35 U.S.C. §112, first paragraph, regarding enablement should be withdrawn

The rejection of all claims under 35 U.S.C. §112, first paragraph, for assertedly lacking enablement should be withdrawn because undue experimentation is not required to practice the claimed invention. It is completely routine in the art to (1) make mutations or deletions in nucleotide sequences, (2) express nucleotide sequences in host cells, (3) test the expressed protein for activity, and (4) generate antibodies to proteins. The Examiner does not appear to dispute these general facts.

The primary basis of the rejection appears to be that the genus of polypeptides referenced in the claim includes variants and fragments including having deletion, substitution or insertion of one or plural amino acid residues in the sequence. However, Applicants note that the breadth of the genus of the claimed invention is not unlimited. The genus is characterized structurally by the hybridization conditions recited in the claims and additionally by the structural feature of retaining a cysteine backbone, and functionally by retaining the ability to alter bone density.

"The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention." Johns Hopkins Univ. v. Cellpro, Inc., 152 F.3d 1342, 47 U.S.P.Q.2D 1705 (Fed. Cir. 1998). "The enablement requirement is

met if the description enables any mode of making and using the invention." Johns Hopkins Univ., *supra*. (emphasis added).

The modification of polynucleotides and the expression of variant polypeptides was routine in the art. For example, a number of standard laboratory manuals describe techniques that had been used for a decade prior to the filing date of the present application to make modifications to polynucleotides, transform or transfect host cells with such polynucleotides, and recombinantly produce polypeptides. See for example, *Current Protocols in Molecular Biology*. Ausubel, F.M. et al. eds., Wiley, Interscience New York (1987), which is updated regularly, or *Molecular Cloning: A Laboratory Manual*, 2nd ed., Sambrook, J., Fritsch, E. and Maniatis,T. Cold Spring Harbor Press, Cold Spring Harbor, NY (1989). See also more recent texts such as *Principles of Gene Manipulation: An Introduction of Genetic Engineering* 5th ed., Old, R. and Primrose,S., eds., Blackwell Scientific Publications, London (1994), or *Handbook of Molecular and Cellular Methods in Biology and Medicine*, Kaufman,P., Wu,W. and Kim,D, eds. CRC Press, Boca Raton , FL (1995). The preparation of antibodies to polypeptides was also routine in the art as evidenced by *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988) and Antibodies: A Laboratory Manual, E. Harlow and D. Lane, ed., Cold Spring Harbor Laboratory (Cold Spring Harbor, NY, 1988).

Applicants respectfully submit that there is a great deal of guidance in the specification regarding the modification of polynucleotides and the expression of variant polypeptides. For example, in the section describing how to make amino acid modifications to the protein, the specification states that the cysteine backbone of the protein (illustrated in Figure 1) should generally be conserved. See, e.g., page 21, line 7, page 26, line 29-page 27, line 1, and Figure 1. Moreover, the specification provides seven different sequences of native mammalian and variant human cDNA (SEQ ID NOS: 1, 5, 7, 9, 11, 13 and 15, see pages 81-84 of specification), from which one can determine which amino acids and regions are conserved among mammalian species. A sample alignment of the coding regions of these sequences generated using CLUSTAL W (1.83) program is attached hereto as Exhibit A, wherein the conserved residues are indicated at bottom by stars. Earlier versions prior to the filing date (see, e.g., Higgins et al., "Using CLUSTAL for multiple sequence alignments," *Methods Enzymol.*, 266, 383-402 (1996)) could easily have been used to generate a similar alignment, or visual inspection would have yielded the same information.

From this information, one of ordinary skill in the art could make knowledgeable choices regarding modifications; for example, conservative substitutions in the conserved regions are more likely to retain activity, while non-conserved regions are better able to tolerate non-conservative modifications. Similarly, substitutions in the cysteine backbone that affect folding are more likely to reduce activity. Thus, there is ample direction and guidance in the specification regarding correlation between structure and function.

The Examiner relies on the *Wands* test for enablement, and contends that a worker of skill in the art would have to undergo undue experimentation to practice the claimed invention. Applicants respectfully disagree. *Wands* involved screening of large numbers of hybridomas to identify specific hybridomas that fell within the claim limitations. The court in *Wands* indicates that because Wands provided sufficient guidance to make and screen the hybridomas and presented working examples, that the enablement requirement was fulfilled. *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988). *In re Wands* does not hold that a specific number of working examples is required. In reaching a decision, the court in *Wands* considered that the inventor's disclosure provides considerable direction and guidance on how to practice the invention and presents working examples. *Id* at 740. This fact coupled with the high level of skill in the art renders the invention enabled in the courts' opinion. *Id.*

Regarding the Wands factors discussed by the Examiner at pages 6-7 of the Action, the level and knowledge of skill of those in the art is relatively high. The assertion that there is no direction or guidance in the specification is incorrect for the reasons stated above. The statement that working examples are absent is incorrect because, as noted below, there are at least seven different working examples of mammalian cDNAs (including human, variant human, vervet, murine, rat and bovine) in the specification (SEQ ID NOS: 1, 5, 7, 9, 11, 13, and 15). The assertion regarding the complex nature of the invention is not supported by specific reasoning, particularly in view of the fact that the generation of polypeptides and antibodies is quite routine in the art. Thus, proper consideration of the Wands factors requires a conclusion that the claimed invention does not require undue experimentation.

Applicants also disagree with the Examiner's assertion at page 5 of the Action that the hybridization conditions recited in claim 88 are not stringent. Under salt-containing hybridization conditions, the effective melting temperature (Tm) is what determines the

degree of homology between the two DNAs that is required for successful hybridization. One formula for calculating Tm, based on salt content, formamide content and GC content of the DNA, is set forth below:

Effective Tm (Eff Tm) = 81.5 + 16.6(log M [Na+]) + 0.41(%G+C) - 0.72(% formamide)

In general, if one assumes that a 1% mismatch of two DNAs lowers the Tm 1.4°C, then for SEQ ID NO: 1 these calculations estimate that about 80% homology is required for successful hybridization under the wash conditions recited in claim 88. While the scope of the claims is not limited by any theoretical calculations such as this, this relatively high estimated homology contradicts the position that the hybridization conditions are of the low stringency suggested by the Examiner.

The Examiner has not provided specific reasons why a genus of polypeptides encoded by polynucleotides 90% identical to the exemplified sequences in the specification is not enabled; the rejection noted above regarding stringency conditions does not apply to claim 89. Applicants also note that the scope of the polynucleotides recited in claim 89 parallels issued claims in grandparent application U.S. Patent No. 6,395,511. Claim 1 of this patent is set forth below:

> 1. An isolated nucleic acid molecule comprising a polynucleotide having at least 90% identity with the full length of SEQ ID NO:1 or the complement thereof, wherein said nucleic acid molecule encodes a protein which specifically binds to at least a human bone morphogenic protein selected from the group consisting of bone morphogenic protein 5 and bone morphogenic protein 6.

Having adequately described and enabled a novel protein that is 90% identical to a reference sequence, it would be routine experimentation to make antibodies to such proteins. For all of these reasons, one of ordinary skill in the art would be able to make and use the presently claimed invention without undue experimentation, and the rejection for lack of enablement should be withdrawn.

B. The rejection under 35 U.S.C. §112, first paragraph, regarding written description should be withdrawn

The rejection of all claims under 35 U.S.C. §112, first paragraph, for assertedly lacking written description should be withdrawn because (1) Applicants have provided a representative number of species for the genus, (2) Applicants have provided relevant identifying characteristics of the genus through structure correlated with function, and (3) Patent Office training materials and issued patents show that the Patent Office approves of the description of a genus in terms of the language recited in the claims.

There are two alternatives for satisfying the written description requirement for a genus: description of a representative number of species, or disclosure of relevant identifying characteristics of the genus. MPEP §2163 states that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above).

The Examiner is incorrect in stating that Applicants have provided "one species." Page 7 of the Action. According to the written description guidelines for examination, analysis of a recited genus requires, first, that the Examiner determine if there is a representative number of species implicitly or explicitly disclosed. "What is a representative number of species depends on whether one of ordinary skill in the art would recognize the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed or claimed." [See page 3 of the Written Description Guidelines for Examination.] Applicants have provided seven different mammalian sequences, including three different naturally occurring variants of the human sequence of "Beer" and the vervet, mouse, rat, and cow sequence of "Beer". The human and rat sequences are about 87% identical; the human and

murine sequences are about 88% identical, and the human and vervet sequences are about 97% identical. Thus, Applicants have provided multiple species that are representative of the breadth of the genus of claim 88 and that even exceed the breadth recited in claim 89 (90% identical). In view of the number of species mentioned above, Applicants submit that a "representative number" of species are described and the specification fully supports the genus recited in the claims. For this reason alone, the written description rejection may properly be withdrawn.

The Examiner is also incorrect in stating at page 7 of the Action that the "specification does not define any structural features commonly possessed by members of the genus that distinguish them from others." Applicants have provided relevant structural features and other identifying characteristics. The specification describes the structure of seven different sequences. The specification provides comparisons between those sequences (falling within the genus) and other sequences, such as Dan, Gremlin and Cerberus, that fall outside the claimed genus. The specification discloses functional characteristics such as biological activity of altering bone density and bone mineral content. The specification also describes a correlation between structure and function. The claims recite structural features through hybridization language or percent identity language in addition to the cysteine backbone, as well as functional features such as ability to alter bone density. Moreover, the specification discloses at least two cDNA sequences (i.e., human and vervet) that would hybridize under high stringency conditions and would function as described in the claims. Accordingly, one of skill in the art would expect that the rat and murine cDNA sequences provided in the specification would also hybridize under high stringency conditions and function as described in the claims. Support for exemplary high stringency conditions can be found in the specification at page 4, lines 14-19 and at page 28, lines 11-20. For all of the reasons discussed above with respect to enablement, there is a correlation between the structural characteristics and the functional characteristics. Thus, the claims recite sufficient identifying characteristics to distinguish the claimed genus.

According to the Revised Interim Written Description Guidelines Training Materials (1999), hybridization conditions are a suitable way to describe the structural characteristics of a genus of polynucleotides. See Example 9, which states:

> a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.
>
> Conclusion: The claimed invention is adequately described.

The written description training materials also state that percent identity is a suitable way to describe the structural characteristics of a genus of polypeptides. See Example 14, which states:

> The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.

In response to the Examiner's comment regarding the different factual basis for the claims of U.S. Patent No. 6,562,949, Applicants have simply cited this patent as proof that the Patent Office has previously taken the position that a *genus of antibodies* is enabled and adequately described by language that refers to a genus of polypeptides. For the reasons discussed herein, the genus of antibodies recited in the present claims is enabled and adequately described.

Thus, the applicable training materials from the Patent Office and other issued patents demonstrate that it is entirely appropriate to use language such as the hybridization language or percent identity recited in the present claims to describe a genus of compounds. Applicants have not only provided a representative number of species but also sufficient identifying characteristics to define the genus. Moreover, because the specification provides a reference sequence (e.g., SEQ ID NOs: 1, 5, 7, 9, 11, 13, or 15) and describes a procedure to identify variants of said reference sequence (i.e., by hybridrization under stringent

conditions or percent identity), one of skill in the art would realize from the specification that the inventors were in possession of the invention at the time of filing. For all of these reasons, there is adequate description of the claimed genus and the written description requirement should be withdrawn.

C. The obviousness-type double patenting rejection

Applicants will file a terminal disclaimer upon an indication that the claims are otherwise allowable.

D. Conclusion

In view of the above remarks, applicants believe all pending claims are in condition for allowance. Please charge any deficiency in the fees to Deposit Account No. 13-2855.

Dated: August 21, 2007

Respectfully submitted,

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EXHIBIT A, page 1

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Human           AGAGCCTGTGCTACTGGAAGGTGGCGTGCCCTCCTCTGGCTGGTACCATGCAGCTCCCAC 60
V10I            AGAGCCTGTGCTACTGGAAGGTGGCGTGCCCTCCTCTGGCTGGTACCATGCAGCTCCCAC 60
P38R            AGAGCCTGTGCTACTGGAAGGTGGCGTGCCCTCCTCTGGCTGGTACCATGCAGCTCCCAC 60
Vervet          ----------------------------------------------ATGCAGCTCCCAC 13
Mouse           ----------------------------------------------ATGCAGCCCTCAC 13
Rat             ---------------GAGGACCGAGTGCCCTTCCTCCTTCTGGCACCATGCAGCTCTCAC 45
Bovine          ------------------------------------------------------------

Human           TGGCCCTGTGTCTCGTCTGCCTGCTGGTACACACAGCCTTCCGTGTAGTGGAGGGCCAGG 120
V10I            TGGCCCTGTGTCTCATCTGCCTGCTGGTACACACAGCCTTCCGTGTAGTGGAGGGCCAGG 120
P38R            TGGCCCTGTGTCTCGTCTGCCTGCTGGTACACACAGCCTTCCGTGTAGTGGAGGGCCAGG 120
Vervet          TGGCCCTGTGTCTTGTCTGCCTGCTGGTACACGCAGCCTTCCGTGTAGTGGAGGGCCAGG 73
Mouse           TAGCCCCGTGCCTCATCTGCCTACTTGTGCACGCTGCCTTCTGTGCTGTGGAGGGCCAGG 73
Rat             TAGCCCCTTGCCTTGCCTGCCTGCTTGTACATGCAGCCTTCGTTGCTGTGGAGAGCCAGG 105
Bovine          ------------------------------------------------------------

Human           GGTGGCAGGCGTTCAAGAATGATGCCACGGAAATCATCCCCGAGCTCGGAGAGTACCCCG 180
V10I            GGTGGCAGGCGTTCAAGAATGATGCCACGGAAATCATCCGCGAGCTCGGAGAGTACCCCG 180
P38R            GGTGGCAGGCGTTCAAGAATGATGCCACGGAAATCATCCGCGAGCTCGGAGAGTACCCCG 180
Vervet          GGTGGCAGGCCTTCAAGAATGATGCCACGGAAATCATCCCCGAGCTCGGAGAGTACCCCG 133
Mouse           GGTGGCAAGCCTTCAGGAATGATGCCACAGAGGTCATCCCAGGGCTTGGAGAGTACCCCG 133
Rat             GGTGGCAAGCCTTCAAGAATGATGCCACAGAAATCATCCCGGGACTCAGAGAGTACCCAG 165
Bovine          ---------------AGAATGATGCCACAGAAATCATCCCCGAGCTGGGCGAGTACCCCG 45
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Human           AGCCTCCACCGGAGCTGGAGAACAACAAGACCATGAACCGGGCGGAGAACGGAGGGCGGC 240
V10I            AGCCTCCACCGGAGCTGGAGAACAACAAGACCATGAACCGGGCGGAGAACGGAGGGCGGC 240
P38R            AGCCTCCACCGGAGCTGGAGAACAACAAGACCATGAACCGGGCGGAGAACGGAGGGCGGC 240
Vervet          AGCCTCCACCGGAGCTGGAGAACAACAAGACCATGAACCGGGCGGAGAATGGAGGGCGGC 193
Mouse           AGCCTCCTC------CTGAGAACAACCAGACCATGAACCGGGCGGAGAATGGAGGCAGAC 187
Rat             AGCCTCCTCAGGAACTAGAGAACAACCAGACCATGAACCGGGCCGAGAACGGAGGCAGAC 225
Bovine          AGCCTCTGCCAGAGCTG---AACAACAAGACCATGAACCGGGCGGAGAACGGAGGGAGAC 102
                ******  *           ****** ***************** ***** *****  * *

Human           CTCCCCACCACCCCTTTGAGACCAAAGACGTGTCCGAGTACAGCTGCCGCGAGCTGCACT 300
V10I            CTCCCCACCACCCCTTTGAGACCAAAGACGTGTCCGAGTACAGCTGCCGCGAGCTGCACT 300
P38R            CTCCCCACCACCCCTTTGAGACCAAAGACGTGTCCGAGTACAGCTGCCGCGAGCTGCACT 300
Vervet          CTCCCCACCACCCCTTTGAGACCAAAGACGTGTCCGAGTACAGCTGCCGAGAGCTGCACT 253
Mouse           CTCCCCACCATCCCTATGACGCCAAAGGTGTGTCCGAGTACAGCTGCCGCGAGCTGCACT 247
Rat             CCCCCCACCATCCTTATGACACCAAAGACGTGTCCGAGTACAGCTGCCGCGAGCTGCACT 285
Bovine          CTCCCCACCACCCCTTTGAGACCAAAGACGCCTCCGAGTACAGCTGCCGGGAGCTGCACT 162
                * ******** ** * ***  ******  *  ***************** **********

Human           TCACCCGCTACGTGACCGATGGGCCGTGCCGCAGCGCCAAGCCGGTCACCGAGCTGGTGT 360
V10I            TCACCCGCTACGTGACCGATGGGCCGTGCCGCAGCGCCAAGCCGGTCACCGAGCTGGTGT 360
P38R            TCACCCGCTACGTGACCGATGGGCCGTGCCGCAGCGCCAAGCCGGTCACCGAGCTGGTGT 360
Vervet          TCACCCGCTACGTGACCGATGGGCCGTGCCGCAGCGCCAAGCCAGTCACCGAGTTGGTGT 313
Mouse           ACACCCGCTTCCTGACAGACGGCCCATGCCGCAGCGCCAAGCCGGTCACCGAGTTGGTGT 307
Rat             ACACCCGCTTCGTGACCGACGGCCCGTGCCGCAGTGCCAAGCCGGTCACCGAGTTGGTGT 345
Bovine          TCACCCGCTACGTGACCGATGGGCCGTGCCGCAGCGCCAAGCCGGTCACCGAGCTGGTGT 222
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EXHIBIT A, page 2

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Human           GCTCCGGCCAGTGCGGCCCGGCGCGCCTGCTGCCCAACGCCATCGGCCGCGGCAAGTGGT 420
V10I            GCTCCGGCCAGTGCGGCCCGGCGCGCCTGCTGCCCAACGCCATCGGCCGCGGCAAGTGGT 420
P38R            GCTCCGGCCAGTGCGGCCCGGCGCGCCTGCTGCCCAACGCCATCGGCCGCGGCAAGTGGT 420
Vervet          GCTCCGGCCAGTGCGGCCCGGCACGCCTGCTGCCCAACGCCATCGGCCGCGGCAAGTGGT 373
Mouse           GCTCCGGCCAGTGCGGCCCCGCGCGGCTGCTGCCCAACGCCATCGGGCGCGTGAAGTGGT 367
Rat             GCTCGGGCCAGTGCGGCCCCGCGCGGCTGCTGCCCAACGCCATCGGGCGCGTGAAGTGGT 405
Bovine          GCTCGGGCCAGTGCGGCCCGGCGCGCCTGCTGCCCAACGCCATCGGCCGCGGCAAGTGGT 282
                **** ************** ** ** ******************** ****  *******

Human           GGCGACCTAGTGGGCCCGACTTCCGCTGCATCCCCGACCGCTACCGCGCGCAGCGCGTGC 480
V10I            GGCGACCTAGTGGGCCCGACTTCCGCTGCATCCCCGACCGCTACCGCGCGCAGCGCGTGC 480
P38R            GGCGACCTAGTGGGCCCGACTTCCGCTGCATCCCCGACCGCTACCGCGCGCAGCGCGTGC 480
Vervet          GGCGCCCGAGTGGGCCCGACTTCCGCTGCATCCCCGACCGCTACCGCGCGCAGCGTGTGC 433
Mouse           GGCGCCCGAACGGACCGGATTTCCGCTGCATCCCGGATCGCTACCGCGCGCAGCGGGTGC 427
Rat             GGCGCCCGAACGGACCCGACTTCCGCTGCATCCCGGATCGCTACCGCGCGCAGCGGGTGC 465
Bovine          GGCGCCCAAGCGGGCCCGACTTCCGCTGCATCCCCGACCGCTACCGCGCGCAGCGGGTGC 342
                **** ** *  ** ** ** ************** ** ***************** ****

Human           AGCTGCTGTGTCCCGGTGGTGAGGCGCCGCGCGCGCGCAAGGTGCGCCTGGTGGCCTCGT 540
V10I            AGCTGCTGTGTCCCGGTGGTGAGGCGCCGCGCGCGCGCAAGGTGCGCCTGGTGGCCTCGT 540
P38R            AGCTGCTGTGTCCCGGTGGTGAGGCGCCGCGCGCGCGCAAGGTGCGCCTGGTGGCCTCGT 540
Vervet          AGCTGCTGTGTCCCGGTGGTGCCGCGCCGCGCGCGCGCAAGGTGCGCCTGGTGGCCTCGT 493
Mouse           AGCTGCTGTGCCCCGGGGGCGCGGCGCCGCGCTCGCGCAAGGTGCGTCTGGTGGCCTCGT 487
Rat             AGCTGCTGTGCCCCGGCGGCGCGGCGCCGCGCTCGCGCAAGGTGCGTCTGGTGGCCTCGT 525
Bovine          AGCTGTTGTGTCCTGGCGGCGCGGCGCCGCGCGCGCGCAAGGTGCGCCTGGTGGCCTCGT 402
                ***** **** ** ** ** *  ********* ************* *************

Human           GCAAGTGCAAGCGCCTCACCCGCTTCCACAACCAGTCGGAGCTCAAGGACTTCGGGACCG 600
V10I            GCAAGTGCAAGCGCCTCACCCGCTTCCACAACCAGTCGGAGCTCAAGGACTTCGGGACCG 600
P38R            GCAAGTGCAAGCGCCTCACCCGCTTCCACAACCAGTCGGAGCTCAAGGACTTCGGGACCG 600
Vervet          GCAAGTGCAAGCGCCTCACCCGCTTCCACAACCAGTCGGAGCTCAAGGACTTCGGTCCCG 553
Mouse           GCAAGTGCAAGCGCCTCACCCGCTTCCACAACCAGTCGGAGCTCAAGGACTTCGGGCCGG 547
Rat             GCAAGTGCAAGCGCCTCACCCGCTTCCACAACCAGTCGGAGCTCAAGGACTTCGGACCTG 585
Bovine          GCAAGTGCAAGCGCCTCACTCGCTTCCACAACCAGTCCGAGCTCAAGGACTTCGGGCCCG 462
                ****************** ***************** *****************  * *

Human           AGGCCGCTCGGCCGCAGAAGGGCCGGAAGCCGCGGCCCCGCGCCCGGAGCGCCAAAGCCA 660
V10I            AGGCCGCTCGGCCGCAGAAGGGCCGGAAGCCGCGGCCCCGCGCCCGGAGCGCCAAAGCCA 660
P38R            AGGCCGCTCGGCCGCAGAAGGGCCGGAAGCCGCGGCCCCGCGCCCGGAGCGCCAAAGCCA 660
Vervet          AGGCCGCTCGGCCGCAGAAGGGCCGGAAGCCGCGGCCCCGCGCCCGGGGGGCCAAAGCCA 613
Mouse           AGACCGCGCGGCCGCAGAAGGGTCGCAAGCCGCGGCCCGGCGCCCGGGGAGCCAAAGCCA 607
Rat             AGACCGCGCGGCCGCAGAAGGGTCGCAAGCCGCGGCCCCGCGCCCGGGGAGCCAAAGCCA 645
Bovine          AGGCCGCGCGGCCGCAAACGGGCCGGAAGCTGCGGCCCCGCGCCCGGGGCACCAAAGCCA 522
                ** **** ******** * *** ** **** ******* ******** *  *********

Human           ACCAGGCCGAGCTGGAGAACGCCTACTAGAGCCCGCCCGCGCCCCTCCCCACCGGCGGGC 720
V10I            ACCAGGCCGAGCTGGAGAACGCCTACTAGAGCCCGCCCGCGCCCCTCCCCACCGGCGGGC 720
P38R            ACCAGGCCGAGCTGGAGAACGCCTACTAGAGCCCGCCCGCGCCCCTCCCCACCGGCGGGC 720
Vervet          ATCAGGCCGAGCTGGAGAACGCCTACTAG------------------------------- 642
Mouse           ACCAGGCGGAGCTGGAGAACGCCTACTAGAG---------------------------- 638
Rat             ACCAGGCGGAGCTGGAGAACGCCTACTAG------------------------------- 674
Bovine          GCCGGGCCGA---------------------------------------------------- 532
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